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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/679,478	10/07/2003	Steven P. Adams	14406-003006	6640

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EXAMINER
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AULAKH, CHARANJIT

ART UNIT	PAPER NUMBER
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1625

MAIL DATE	DELIVERY MODE
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12/03/2007

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

## Office Action Summary

Application No.

10/679,478

Applicant(s)

ADAMS ET AL.

Examiner

Charanjit S. Aulakh

Art Unit

1625

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 04 October 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-22 is/are pending in the application.
- 4a) Of the above claim(s) 3, 4 and 11-13 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1, 2, 5-10 and 14-22 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date 10/7/03.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_.

### DETAILED ACTION

1. According to paper filed on Oct. 4, 2007, the applicants have elected group I ( compound 1400 as elected species ) in response to restriction requirement for further prosecution. The applicants have also withdrawn claims 3, 4 and 11-13 from further consideration.

2. Claims 1, 2, 5-10 and 14-22 are now pending in the application.

#### ***Claim Rejections - 35 USC § 112***

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1, 2, 5-10 and 14-22 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In independent claim 1, the applicants have added -CH<sub>2</sub>- value for the variable Y. However, this value is not present in the specification. Similarly, the applicants have added hydrogen for the value of variable R<sub>3</sub> which is not present in the specification.

5. Claims 1, 2, 5-10 and 14-22 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use

the invention. The following eight different factors (see Ex parte Foreman, 230 USPQ at 547; Wands, In re, 858.F. 2d 731, 8 USPQ 2d 1400, Fed. Cir. 1988) must be considered in order for the specification to be enabling for what is being claimed:

Quantity of experimentation necessary, the amount of direction or guidance provided, presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability and the breadth of claims. In the instant case, the specification is not enabling based on at least four of the above mentioned eight different factors such as quantity of experimentation necessary, the amount of direction or guidance provided, presence of working examples, state of the prior art, unpredictability and the breadth of claims.

In regard to lack of enablement issue of instant claims 1, 2, 5-10 and 14-22 for derivatives of instant compounds of formula (I), there is no teaching or guidance present in the specification for preparing any specific derivative such as esters, prodrugs, metabolites and residues as defined in the specification on page 16 ( see lines 12-19 ).

In regard to prodrug forms, there is no teaching or guidance present in the specification for preparing specific types of prodrug form such carboxylic acid esters, amino acid or amide esters, phosphate esters, phosphono esters , sulfate esters etc. There is not even a single working example present in the specification for preparing any type of metabolite, residue or specific prodrug form of instant compounds of formula (I). There is lot of unpredictability in the art for efficacy of different types of prodrug forms of any known compound following their in vivo administration since their efficacy depends upon various factors such as absorption from gut, metabolism by esterases etc. The instant

compounds of formula (I) encompasses hundreds of thousands of compounds based on the values of variables R1-R4, n, Y and X and therefore, in absence of such teachings, guidance, presence of working examples and unpredictability, it would require undue experimentation to select specific types of prodrug forms of instant compounds of formula I which will be effective following in vivo administration.

In regard to enablement rejection of claims 1, 2, 5-10 and 14-22 for cell adhesion inhibitory compound, pharmaceutical composition or methods of treatment, the specification teaches that the instant compounds are antagonists of VLA—dependent cell adhesion in vitro ( see example 67 on page 133 of specification as well as table on pages 135-137 ). However, VLA4 or alpha 4 beta1 integrin is only one of several known integrins involved in cell adhesion ( see page 2, lines 6-22 of specification ). Therefore, the instant compounds will have utility in inhibiting cell adhesion mediated by VLA4 alone and furthermore for treating but not preventing or completely inhibiting cell adhesion. There is no teaching in the specification or prior art that VLA4 –mediated cell adhesion will be maintained in the presence of hundreds of thousands of other drugs such as antimetabolites, antidiabetics etc. The combination of instant compounds with other drugs may actually compromise their inhibitory effect on VLA4-mediated cell adhesion due to drug interaction. There are no working examples present showing efficacy of instant compounds in known animal models of autoimmune diseases, psoriasis, inflammatory diseases and diabetes. The instant compounds of formula (I) encompasses hundreds of thousands of compounds based on the values of variables R1-R4, n, Y and X and therefore, in absence of such teachings, guidance, presence of

working examples and prior art, it would require undue experimentation to demonstrate efficacy of instant compounds in known animal models of autoimmune diseases, psoriasis, inflammatory diseases and diabetes and hence their utility for treating these disorders.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1, 2, 5-10 and 14-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In independent claim 1, the value of variable R2 is not defined and furthermore, the value of variable R4 is defined twice.

Claim 5 recites the limitation "hydrogen or methyl for the value of variable R2" in claim

1. There is insufficient antecedent basis for this limitation in the claim.

### ***Double Patenting***

8. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct

from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement. Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

9. Claims 1, 2, 5-10 and 14-22 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-48 of U.S. Patent No. 6,376,538, cited on applicant's form 1449. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the cited patent anticipate the instant claims when X represents -COOH and R1, R3 and R4 represent alkyl, alkenyl or alkynyl group in the compounds of the cited patent.

10. Claims 1, 2, 5-10 and 14-22 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-38 of U.S.

Patent No. 6,306,804, cited on applicant's form 1449. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the cited patent anticipate the instant claims when Y represents  $-\text{CO}-$  and R1, R3 and R4 represent alkyl, alkenyl or alkynyl group in the compounds of the cited patent.

11. Claims 1, 2, 5-10 and 14-22 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-20 of U.S.

Patent No. 6,552,216. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the cited patent anticipate the instant claims when A represents aliphatic acyl and R2 and R4 represent alkyl group in the compounds of the cited patent.

12. Claims 1, 2, 5-10 and 14-22 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-53 of U.S.

Patent No. 6,630,512. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the cited patent anticipate the instant claims when R1, R3 and R4 represent alkyl, alkenyl or alkynyl group in the compounds of the cited patent.

13. Claims 1, 2, 5-10 and 14-22 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-34 of U.S.

Patent No. 6,624,152. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the cited patent anticipate the instant claims when X represents  $-\text{COOH}$ , Y represents  $-\text{CO}$  and R1, R3 and R4 represent alkyl, alkenyl or alkynyl group in the compounds of the cited patent.



14. Claims 1, 2, 5-10 and 14-22 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-9 of U.S. Patent No. 7,001,921. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the cited patent anticipate the instant claims when X represents  $-\text{COOH}$ , Y represents  $-\text{CO}$  and R1, R3 and R4 represent alkyl, alkenyl or alkynyl group in the compounds of the cited patent.

15. Claims 1, 2, 5-10 and 14-22 are objected for containing non-elected subject matter.

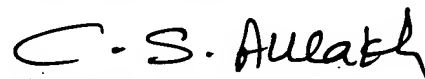
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charanjit S. Aulakh whose telephone number is (571)272-0678. The examiner can normally be reached on Monday through Friday, 8:30 A.M. to 5:00 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on (571)272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Primary Examiner  
Art Unit 1625